Changes in mean values of thyroid function tests in patients receiving diclofenac and control group

Thyroid test	Group	Time after start of study			Normal range
		0	1 month	2 months	
Triiodothyronine uptake %	Diclofenac	108	105	107	
	Control	111	104	112	
Tetraiodothyronine (radioimmunoassay) (nmol/l)	Diclofenac	135	133	126	65–185 nmol/l
	Control	132	134	128	
Free thyroxine index	Diclofenac	125	127	121	65–185
	Control	119	132	133	
Thyroid stimulating hormone (mu/l)	Diclofenac	4·5	4·1	4·1	1·0–10·0 μU/ml
	Control	5·3	4·6	4·4	

Conversion: SI to traditional units—Tetraiodothyronine: 1 nmol/l ≈ 65·1 ng/100 ml.

steroidal anti-inflammatory medication for one month. Then all had their original medication for a second month. Thyroid function tests were done at the onset and after one and two months.

To date a total of 26 patients (all but five with rheumatoid arthritis) have entered the study and 12 patients have completed. A further six have completed the four week assessment. Six patients have been withdrawn: two for administrative reasons; two had initial high thyroid stimulating hormone concentrations; one responded poorly to therapy; and one felt sick. All were in the diclofenac group. Another two patients responded so well to the first treatment (diclofenac) that it was not felt justifiable to revert to their original treatment, although tests were repeated after two months. This preliminary report is based on the following: a control group with 11 patients who had first and second assessments and eight patients who had all three assessments; and a diclofenac group with seven patients who had first and second assessments and four patients who had all three assessments. The results are shown in the table.

It is clear from these figures that diclofenac has no clinically important effect on thyroid function tests and certainly no different effect from a range of non-steroidal anti-inflammatory drugs.

The object of this study is to assess whether diclofenac has any clinically relevant effect on thyroid function tests. Our preliminary results suggest that it does not. It is our intention to publish the full results and details of our study when complete, but the recent report in your journal from Dr R Taylor and others (4 October, p 911) suggesting that fenclofenac not only displaces thyroxine from its binding site, but has a thyroxine-like action on the pituitary gland prompts us to report that another phenylacetic acid derivative, diclofenac, does not have this effect, suggesting that the phenylacetic acid part of the molecule is not relevant.

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[1] Isaacs AJ, Monk BE. *Lancet* 1980;i:267.
[2] Ratcliffe WA, Hazelton RA, Thomson JA. *Lancet* 1980;i:432.

Effect of beta-blockers on thyroid hormone

SIR,—We have read with interest the report by Dr Paul Heyma and his colleagues (5 July, p 24) of the effect of D- and DL-propranolol on plasma triiodothyronine (T3) concentrations in euthyroid volunteers and hypothyroid patients receiving L-thyroxine (T4) replacement. They state that the mechanism by which both isomers of propranolol inhibit conversion of T4 to T3 is unclear. Having shown this metabolic inhibition to be unrelated to β-adrenergic blocking activity they suggest that the membrane-stabilising effect of propranolol may be responsible. This is unlikely, as the propranolol concentrations required at a cell membrane for such an effect are considerably higher than those necessary for beta-blockade[1] and were probably not attained by the dosing regimen used by Heyma *et al.* Another beta-blocker, atenolol, is as effective as propranolol in controlling thyrotoxic symptoms, but while T3 concentration fell during propranolol treatment no change was seen during treatment with atenolol.[2]

We have recently examined the effects of propranolol and metoprolol on the clearance of antipyrine, a compound which, like thyroxine, is metabolised in the liver (observations reported at World Conference on Clinical Pharmacology and Therapeutics, 1980). In five healthy volunteers propranolol lowered antipyrine clearance by 38% and metoprolol by 18%. The influence of the beta-blockers on hepatic blood flow is of little consequence here because the clearance of antipyrine is independent of its rate of delivery to the liver.

One possible explanation for the differential effects of beta-blockers on thyroid hormone and antipyrine metabolism might be related to their lipid solubilities and thus affinities for cytochrome p-450. The stronger the binding of one compound to cytochrome p-450 the greater might be its potential for inhibiting the metabolism of another competing for the same cytochrome site. Propranolol is the most lipid soluble of these beta-blockers, metroprolol occupying an intermediate position; and both practolol and atenolol have very low lipid solubilities.

A recent report by Dr D A Henry and others (20 September, p 775) showed antipyrine clearance in humans to be lowered by cimetidine but not by ranitidine. These observations are in keeping with the hypothesis that metabolic inhibition might be related to lipid solubility as cimetidine is markedly lipid soluble whereas ranitidine is not.[3]

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[1] Paterson JW. In: Burley DM, Frier JH, Rondel RK, Taylor SH, eds. *New perspectives in beta-blockade.* Horsham: Ciba Laboratories, 1973:97-106.
[2] Nilsson OR, Karlberg BE, Kagedal B, Tegler L, Almqvist S. *Acta Med Scand* 1979;**206**:21-25.
[3] Bell AJ, Gower AJ, Martin LE, Mills ENC, Smith WP. *Biochem Soc Trans* (in press).

Two lessons about rabies

SIR,—I am afraid that the two lessons Dr Dennis Parker wishes us to learn after an encounter with a dog bite abroad in a potentially rabid area are neither practical nor wise (18 October, p 1074). Firstly, trying to locate a dog can be difficult enough in this country let alone in a foreign one. Secondly, a visitor abroad can only avail himself of the treatment that is offered to him. Searching for the safe human diploid cell vaccine if not locally available is difficult and time consuming even for a medical practitioner, as Dr Parker found out for himself.

The following recommendations in the order listed would be more appropriate for a visitor in a foreign country:
(1) wash the wound immediately with a liberal amount of water;
(2) begin at once prophylactic antirabies treatment in whatever form available;
(3) report the incident to the authorities;
(4) if there is any risk of rabies and the human diploid cell vaccine is not available then make arrangements to return home as soon as possible. In case of children and severe bites it is always wise to do so. There is always another day for a holiday abroad.

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SIR,—Dr D Parker is wise to beware of the rabid dog (18 October, p 1074). May I add two further points?

Firstly, vigorous cleansing of the wound at once with copious soap and water is all important. Where the bite has "scarcely penetrated the skin" this may well be sufficient treatment.

Secondly, the Merieux human diploid cell vaccine may be given intradermally, with a good antibody response. This is more economical, an important factor where the drug is costly and may be in short supply. Four separate injections of 0·1-0·2 ml, one into each limb, given when the patient first presents, is sufficient to give satisfactory antibody levels.[1] We have found that disposable "insulin" syringes and No 25 needles are suitable, and we use the intradermal route for both prophylaxis and postexposure treatment.

I would not wish to be the one to attempt capture of the suspect animal. The rural Thai speak of good dogs and mad dogs and commonly destroy the latter forthwith. There is perhaps something to be said for this.

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[1] Turner GS, Aoki FY, Nicholson KG, Tyrrell DAJ, Hill LE. *Lancet* 1976;i:1379-81.

Do housemen take an adequate drinking history?

SIR,—The study by Dr I G Barrison and others (18 October, p 1040)—and in particular their application of the terms "accurate" to the numerical and "inaccurate" to the descriptive estimates by housemen of their patients' drinking habits—implies that an individual's assessment of his alcohol consumption can be relied on.

The relationship between the amounts of alcohol which people say they drink and which they actually drink is, however, very ill defined; heavy drinkers are especially poor witnesses and show a strong tendency to underestimate their alcohol intake.[1] This difficulty casts some doubt on the usefulness of recording a patient's quantitative assessment of his alcohol consumption in the case notes; indeed, it suggests